

REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claim 16 has been amended to insert --cyclodextrin complex -- and to delete "Insecticidal composition". This amendment is supported in the as-filed specification.

Claims 17 – 24 have also been amended to insert -- cyclodextrin complex -- and delete "composition".

The claims presently pending in the application are 16 – 24.

CLAIM INTERPRETATION

The interpretation of claim 16 as recited by the Examiner is correct and corresponds to the meaning applicant intended for the claims.

CLAIM REJECTION UNDER 35 USC § 102(b)

Claims 16-18, 20, 21 and 24 were rejected under 35 USC 102(b) as being anticipated by Mifune et al. (US 3,846,551),

The Examiner stated that Mifune et al. "*disclose examples wherein a pyrethroid, cyclodextrin and piperonyl are well kneaded to form a paste (formulation example 7). Cyclodextrin complexes are known to form by kneading with other components (...) Therefore, the compositions according to Formulation Example 7 would comprise both the pyrethroid and the synergist complexed with cyclodextrin since they were well kneaded in the presence of cyclodextrin in water.*"

The formulation of Example 7 of the cited reference illustrates that the preformed interacted compound of pyrethroid and the beta-cyclodextrin is mixed with piperonyl butoxide, stearic acid, Tween 60 and Span 60. Therefore, the Mifune et al. reference describes that an initial complex is formed by the pyrethroid and the cyclodextrin. The kneading of this pre-formed (initial) complex with excipients (i.e. stearic acid, Tween 60 and Span 60) and PBO lead to a paste formulation. However, the presence of all such

ingredients, make it very unlikely that the PBO is included in the cyclodextrin cavity, even more so considering that the cavities are already occupied by the pyrethroid.

While the Applicant agrees that kneading is a known method for preparing an inclusion complex, in order to be effective it needs particular operative conditions (see Mifune, col. 4, lines 1-19) in terms of time, temperature and component ratios which are not the same as those required by the kneading for the mere purpose of preparing a paste formulation (as it is described in the cited Example 7).

Furthermore it is also known that, beyond kneading, alternative methods (such as co-evaporation or co-precipitation) are available, which are much more effective for preparing an inclusion complex. The lower efficiency of kneading versus the co-evaporation method for preparing an inclusion complex is well known in the art. (As an example of such knowledge, the Examiner is requested to review the attached reference Veiga et al. J. Incl. Phenom. & Macrocycl. Chem. 2005, 53, 77-83; in particular see page 81, Fig. 4 and right col., lines 10-23).

Therefore, while it is well-evidenced that the double inclusion complex of the claimed invention is formed by the co-precipitation method according to the instant specification (see § [0026]-[0028]), Mifune et al. do not provide any evidence that the inclusion complex could be obtained under the kneading conditions described in Example 7.

The formation of the double inclusion complex is significantly more complicated than the formation of a single inclusion complex.

There is no experimental evidence in the cited reference that a double inclusion complex pyrethroid-PBO in CD is formed simply by means of kneading. If the formation of an inclusion complex by kneading -under suitable operating conditions- CD, a pyrethroid and PBO in the presence of a suitable amount of water is rather unlikely and unpredictable, a PBO inclusion complex cannot be obtained by kneading the pre-formed inclusion complex (having the cavities already occupied) in the presence of several other components (i.e. surfactants).

Nevertheless, even assuming that a cyclodextrin complex is formed under the conditions referred to in the formulation of Example 7, this complex would have incorporated in its cavity not only the pyrethroid but also the additional kneaded ingredients, that is stearic acid, Tween 60, Span 60 and PBO. A complex (assuming its feasibility) incorporating all of these ingredients, in its cavities, is altogether different from the claimed double inclusion complex and cannot be said to anticipate or render obvious the subject matter of the pending claims.

It is evident that there is no disclosure of a complex with both the active ingredient (pyrethroid) and the synergist compound present in the Mifune et al disclosure.

Therefore, since amended claims 16-18, 20-21 and 24 clearly distinguish over the teaching of Mifune et al. by a preponderance of the evidence, the Examiner has failed to establish a *prima facie* case of anticipation. Since the rejection has been overcome, its withdrawal is solicited.

CLAIM REJECTION UNDER 35 USC § 103

Claims 16-24 stand rejected under 35 USC 103(a) as being unpatentable over Mifune et al. (US 3,846,551) and Szejtli (US 4,524,068). This rejection is respectfully traversed.

Notably, the Examiner mentions the disclosure made by Biebel et al. (Int. J. Pharmaceutics 2003, 256, 175-181) instead of Mifune et al. while attempting to substantiate his rejection.

Biebel discloses complexation of pyrethrum extract with γ -cyclodextrin. Biebel also teaches that pyrethrins can benefit from the use of synergists, such as PBO. Biebel also teaches that a synergist component may also benefit from a complexation with cyclodextrins.

Szejtli teaches that a synergist (such as PBO) can be complexed with cyclodextrins which results in increased solubility.

The disclosures made by Mifune and Szejtli were known to the Applicant and these references are cited at paragraph [0007] of the instant specification.

The Examiner acknowledges that *“Biebel and Szejtli do not explicitly disclose jointly complexing the pyrethrin or pyrethroid and the synergist with cyclodextrin, as instantly claimed”*.

The combination of teachings of Biebel et al., (a pyrethrin can be complexed with cyclodextrin and the synergist can be complexed with cyclodextrin) may suggest, at most, to one of ordinary skill in the art how to arrive at a mixture of pyrethrin/CD complex with a synergist/CD complex. This mixture is decidedly different and readily distinguishable from the claimed double inclusion complex.

Notably, Biebel teaches that the pyrethrum/CD complex used in combination with PBO showed practically the same efficiency as the mixture of pyrethrum and PBO (both not complexed)(see Biebel pages 179 and 180).

Accordingly, the combination of the teachings of Biebel with those of Szejtli may merely suggest to one of ordinary skill in the art the use of a CD complexed pyrethroid in combination with a CD complexed synergist.

It becomes evident that the double inclusion complex of the claimed invention is neither taught nor suggested, nor is it derivable, from a combination of the teachings of Biebel and Szejtli. In addition, it remains fully undisclosed and not derivable at all from the cited references, the entirely unexpected improvement in insecticidal effectiveness of the claimed complexed composition, which is strictly due and connected to the differential release of the two components.

In addition the synergistic insecticide activity of the claimed CD complex remains fully undisclosed and not derivable at all from the cited art taken alone or in combination. Specifically, the NMR spectroscopic data analysis submitted as Annex 2 with the response of August 24, 2010, shows a sustained release for the active pyrethroid of the complex and an earlier and fast release of more than 90% of the PBO component. The earlier/fast release of the PBO inhibits the detoxification enzymes of the insects, while the sustained release of the pyrethroids exerts an action on the insects which have been pre-sensitized by PBO providing a synergistic disinfestation.

The differential release which is experimentally reported by Bingham G. et al *Pest Manag. Sci.* 2007, 63, 276-281 (herewith attached) is strictly connected with the double inclusion complexes of the claimed invention. The tests show that the claimed composition wherein both components (i) and (i) are jointly complexed, is much more effective, far beyond any expectations of the ordinary skilled person, with respect to a mixture of pyrethroids and BTO (CD complexed or not).

In view of the foregoing reasons, claims 16-24 serve to distinguish over the combined teachings of Mifune, Szejtli and Biebel by a preponderance of the evidence. Since the Examiner has failed to establish a case of *prima facie* obviousness, the § 103(a) has been overcome and its withdrawal is solicited.

CONCLUSION

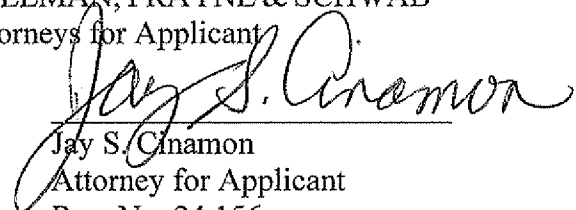
In view of the above, Applicant believes that the restriction requirement should be withdrawn and that the pending Application is in condition for allowance on the grounds that the amendments fully overcome the outstanding rejections.

The issuance of a Notice of Allowance is respectfully solicited.

Please charge any fees that may be due and have not been paid herewith, to our Deposit Account No. 01-0035.

Respectfully submitted,
ABELMAN, FRAYNE & SCHWAB
Attorneys for Applicant

By


Jay S. Cinamon
Attorney for Applicant
Reg. No. 24,156

666 Third Avenue
New York, NY 10017-5621
Tel.: (212) 949-9022
Fax: (212) 949-9190